Tumor Lysate Particle Only Vaccine (TLPO) vs. Tumor Lysate Particle-loaded, Dendritic Cell (TLPLDC) Vaccine to Prevent Recurrence in Resected Stage III/IV Melanoma Patients: Results of a Phase I/IIa Trial

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Background

- The tumor lysate, particle-loaded, dendritic cell (TLPLDC) vaccine is created by loading dendritic cells (DCs) *ex vivo* with yeast cell wall particles (YCWP) with autologous tumor lysate (TL), producing a personalized vaccine.
- The TLPLDC vaccine demonstrated improved 24-month DFS (62.9% vs. 34.8%, p = 0.041) compared to placebo in a per-treatment (PT) analysis in phase IIb trials with 144 patients.[1]
- The tumor lysate (TL) particle only (TLPO) vaccine utilizes a similar mechanism, but with autologous TL-loaded yeast cell wall particles (YCWP), thus reducing production time and cost by eliminating need for dendritic cell (DC) collection and *ex vivo* loading.
- The TLPO vaccine does not require DC harvest, which significantly lowers cost, labor-intensity, and complexity of production when compared to a classical DC vaccine model.
- A silicate cap for the YCWP was developed with a 0.0615 +/- 0.0009-micron (approximately 140 molecular layers) thickness, which facilitated sufficient retention of TL within the YCWP and attracts a monocytic infiltrate.
- Disease free survival (DFS) and overall survival (OS) were compared in patients receiving TLPO versus TLPLDC vaccine in an embedded bridging portion of the overall trial.

Methods

- Patients rendered clinically disease-free after surgery were randomized 2:1 to receive the TLPO or TLPLDC vaccine and followed for recurrence and death.
- Patients had scheduled intradermal inoculations at 0, 1, 2, 6, 12, and 18 months after enrollment.
- Kaplan-Meier and log-rank analysis were used to compare 36-month disease-free survival (DFS) and overall survival (OS) in an intention-to-treat (ITT) analysis, as well as comparing 36-month DFS in exploratory subgroup analyses.

References:

1. Vreeland TJ, Clifton GT, Hale DF, et al. A Phase IIb Randomized Controlled Trial of the TLPLDC Vaccine as Adjuvant Therapy After Surgical Resection of Stage III/IV Melanoma: A Primary Analysis. *Ann Surg Oncol*. Feb 27 2021:1-12. doi:10.1245/s10434-021-09709-1

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The view(s) expressed herein are those of the author(s) and do not reflect the official policy or position of Brooke Army Medical Center, the US Army Medical Department, the Department of the Army, Department of the Air Force, Department of Defense, or the US Government.
The voluntary, fully informed consent of the subjects used in this research was obtained as required by 32 CFR 219 and DODI 3216.02_AFI40-402.

Trial Registration: This is a phase IIb clinical trial registered under NCT02301611.
Ethics Approval: This study was approved by Western IRB, protocol 20141932.

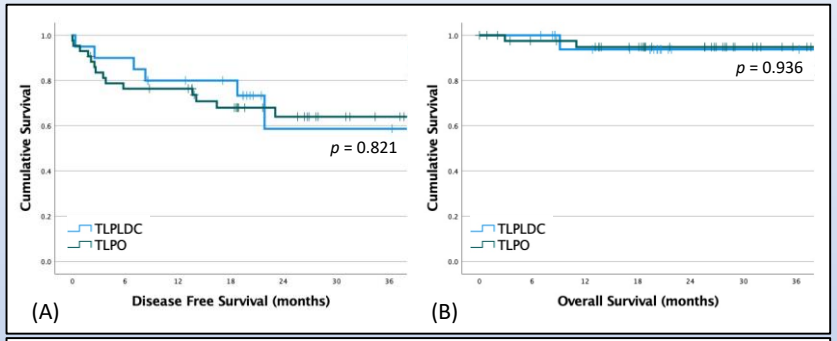

Figure 1. Kaplan Meier curves demonstrating DFS (A) and OS (B) between TLPLDC (n=20) and TLPO (n=43).

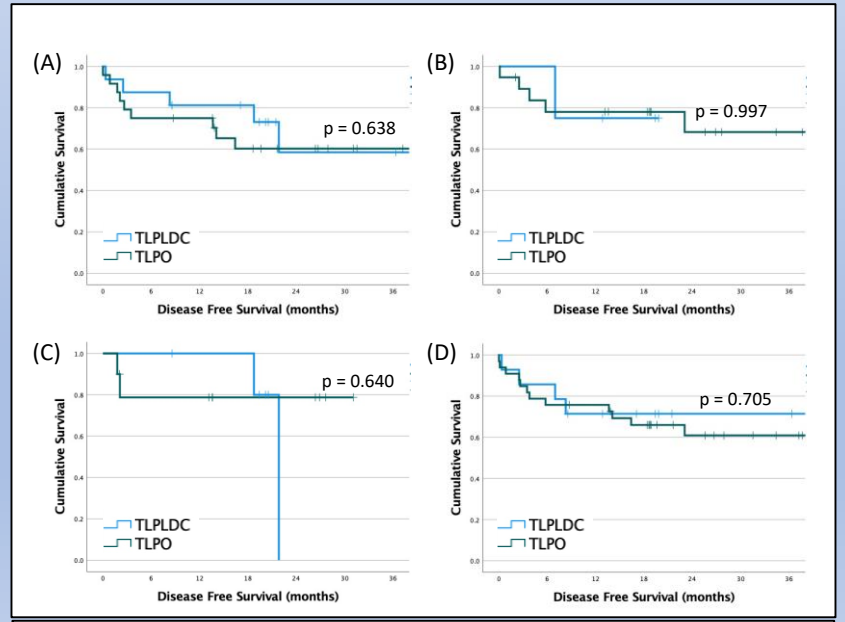

Figure 2. Kaplan-Meier curves of 36-month DFS for Stage III (A) and IV (B) disease, and primary (C) and recurrent (D) disease.

Event	Randomization Arms							
	TLPLDC Vaccine				TLPO Vaccine			
	Definite	Probable	Possible	Total	Definite	Probable	Possible	Total
Cardiac	0	0	0	0	0	0	1	1
Endocrine	0	0	0	0	0	0	1	1
Gastrointestinal	0	1	1	2	1	5	1	7
General disorders and administration site conditions	10	3	1	14	8	0	3	11
Musculoskeletal and connective tissue	0	0	3	3	1	0	0	1
Nervous system	0	1	2	3	1	0	2	3
Respiratory, thoracic, and mediastinal	0	0	0	0	0	0	3	3
Skin and subcutaneous Tissue	9	1	0	10	5	4	2	11
	Total TLPLDC = 32				Total TLPO = 38			
								Overall total = 70

Table 1. Related Adverse Events for TLPLDC (n=20) versus TLPO (n=43) vaccination arms.

Results

- Sixty-three pts were randomized, 43 TLPO and 20 TLPLDC.
- Pts randomized to the TLPO arm were more likely to be female (37.2% vs. 10.0%, $p = 0.026$), but otherwise no significant clinicopathologic differences were identified.
- Of all patients, 31.7% experienced any related AE, for a total of 70 related AEs (38 TLPO, 32 TLPLDC, $p = 0.574$) (Table 1).
- There were 21 total ≥ Grade 3 AEs (17 TLPO, 4 TLPLDC, $p = 0.736$) in 14 patients, but no patient in either group experienced a related ≥ Grade 3 AE.
- A total of 16 SAEs (11 TLPO, 5 TLPLDC, $p = 0.439$) occurred in the study among 10 patients. Only one patient (TLPO vaccination arm) had a related SAE, a pleural effusion requiring an eight-day hospitalization.
- At a median follow-up of 20.5 months, the 36-month DFS (64% vs. 58.7%, $p = 0.821$) and OS (94.8% vs. 93.8%, $p = 0.936$) were equivalent between the TLPO and TLPLDC groups, respectively (Figure 1).
- No differences in 36-month DFS were detected in any exploratory subgroup analysis including:
  - Stage III/IV melanoma (Figure 2)
  - Primary versus recurrent disease (Figure 2)
  - Pre-vaccination immunotherapy and/or CPI vs. none
  - Receipt of G-CSF prior to blood draw versus none

Conclusions

- In a randomized, double-blind phase 2 trial, there were no differences in DFS or OS in clinically disease-free melanoma pts receiving TLPLDC versus TLPO vaccines.
- Given prior efficacy shown with TLPLDC, further testing for efficacy of these two vaccines is warranted in a phase 3 trial.